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## Promacetin in Treatment of Leprosy

### —Progress Report—

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The value of promin, diasone, and sulfetrone in the treatment of leprosy has been reported previously in the medical literature (1, 2, 3). Although any one of these drugs at present might be termed the treatment of choice, the need for more rapidly acting remedies is demonstrated by their exceedingly slow action in effecting a disappearance of the leprosy bacillus from active lesions (4). Furthermore, although these sulfone derivatives are of comparatively low toxicity, they cannot be considered entirely innocuous. Constant medical supervision and periodic laboratory tests are required because of certain toxic manifestations.

Search for a drug of the lowest possible degree of toxicity and of the highest possible therapeutic efficiency in leprosy led to the present clinical evaluation of promacetin.<sup>1</sup> This drug, at one time referred to as Internal Antiseptic 307, is a sulfone closely related chemically to promin, diasone, and sulfetrone, and has been reported to be of relatively low toxicity (5). The explanation for its low toxicity, perhaps, lies in the evidence that it does not break down into diaminodiphenylsulfone. Diaminodiphenylsulfone, the parent substance of promin, diasone, sulfetrone, and promacetin, in comparable doses is a much more toxic product than any one of these derivatives. It is believed, therefore, that the degree of toxicity of the sulfone drugs depends upon the extent to which they break down in the human body into diaminodiphenylsulfone. Also, for promacetin, studies indicated that even with massive doses by mouth the blood level of the drug will seldom attain dangerous proportions. These features of promacetin together with evidence (1) collected at Carville in 1943 that it has antileprotic properties on oral administration, even in

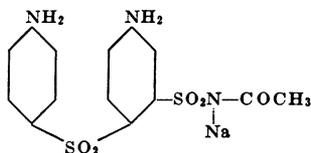
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<sup>1</sup> The drug for this experimental study was supplied by Parke, Davis, and Company, the manufacturers, through Dr. Eugene H. Payne, whose interest stimulated this further investigation.

comparatively small doses, made a further clinical trial of its possibilities in the treatment of leprosy particularly inviting.

Promacetin is sodium 4,4'-diaminodiphenylsulfone-2 acetylsulfonamide. It is a white crystalline compound soluble up to 3 percent in water at room temperature. Its structural formula is as follows:



The therapeutic effectiveness of promacetin compares favorably with sulfapyridine, sulfathiazole, and sulfadiazine in *Streptococcus hemolyticus*, *S. viridans* and *S. pneumoniae* septicemia in mice. Favorable clinical response has been reported in its use for pneumococcus pneumonia in man. Oddly enough, in view of its apparent effectiveness in the acid fast infection of leprosy in humans, it gives no protection against tuberculosis in guinea pigs (6). Adequate clinical trial in human tuberculosis has not been reported.

### Clinical Material

The clinical material for this preliminary evaluation of promacetin included 27 patients—26 of the lepromatous, and 1 of the tubercloid type (table 1). Most of the patients were either moderately or far advanced with unfavorable prognoses and, therefore, exceptionally desirable material for treatment evaluation.

Seventeen patients had received no previous treatment for leprosy, two had received chaulmoogra oil, and eight, sulfones. Of the two patients previously treated with chaulmoogra oil, one had not received any treatment for a period of 11 years and presented nodules and heavy diffuse infiltration; the other had not received treatment for 3 years and likewise showed far advanced manifestations, including extensive confluent nodulation with ulceration. Six patients previously treated with sulfones (promin or diasone) showed only residual

Table 1. Classification of clinical material on type of disease, type of lesions, and previous treatment

Previous treatment	Lepromatous			Tubercloid	Total
	Nodules, macules and diffuse infiltration	Macules and diffuse infiltration	Residual		
None.....	10	6	0	1	17
Chaulmoogra oil.....	2	0	0	0	2
Sulfones.....	2	0	6	0	8
Total.....	14	6	6	1	27

lesions and were included in the study because, in spite of marked clinical improvement on sulfones, all continued to show after several years of treatment a significant number of leprosy bacilli in the skin scrapings. The intention was to determine the effect promaceticin might have in the further reduction of the number of bacilli in the skin of these patients. The remaining two sulfone-treated patients showed active leprosy skin lesions consisting of nodules, macules, and diffuse infiltration. One of these represented a clinical relapse; the other, who in addition showed extensive nodular infiltration of the mucous membrane of the palate, tongue and pharynx, represented a clinical progression of the disease several years after the patient had left the hospital and discontinued all treatment against medical advice.

Table 1 further sets forth the type of lesions the patients presented before treatment. Extensive heavy diffuse infiltration, nodules and macules of the skin of the lepromatous type with numerous (4+) or a moderate (3+) number of bacilli present occurred in 13 patients. Moderate diffuse infiltration with associated infiltrated macules showing either numerous, a moderate number, or few (2+) bacilli present occurred in 7 patients. Residual lesions presenting a variable (4+ to 1+ rare) number of bacilli were seen in 6 of the patients previously treated with sulfones, while 2 showed active fresh lesions as already described. The tuberculoid type patient showed plaques and patches of various sizes devoid of bacilli, and a positive lepromin test. All patients, except those showing only residual lesions and the tuberculoid type patient, had extensive involvement of the nasal mucous membrane, and one had involvement of the entire mouth, nasopharynx, and larynx.

## Methods

Since it is known that the drugs so far found to be effective in leprosy must be administered over a long period of time, the dosage of promaceticin was kept comparatively low during the early stages of treatment. Although promaceticin has been reported to be of low toxicity when given for short periods of time, it was felt that in this group of patients, where treatment of long duration was contemplated, chances could not be taken with initial large doses. Consequently, the initial daily oral dose of promaceticin varied from .3 to .5 gm. except for a small number of male patients of good physique who were given an initial daily oral dose of 1.5 gm. Where the initial dose was .3 to .5 gm. the dosage was increased by .3 to .5 gm. every 2 weeks until a total daily dose of 1.5 gm. was reached. Then the dosage was increased by either 1.0 gm. or 1.5 gm. up to a maximum of from 3.0 to 4.0 gm. daily. For those patients who were begun on 1.5 gm. daily the dosage was increased by either 1.0 gm. or 1.5 gm. every 2 weeks until the maximum of from 3.0 to 4.0 gm. was reached.

Promacetin was administered at meal time as has been customary at Carville with all other orally administered sulfones. Similarly, rest periods, during which the drug was withheld, were observed at the same intervals by the promacetin group of patients as those observed routinely by all other patients taking orally administered sulfones. The rest periods were observed for 15 days during the latter part of March, July, September, and December.

Careful initial clinical and laboratory examinations were conducted and clinical photographs taken. For follow-up, a weekly clinical examination was done and clinical photographs taken whenever sufficient improvement had occurred in the skin lesions to make it possible to record such improvement photographically. An erythrocyte and a leucocyte count, hemoglobin determination, and a urinalysis were done on each patient every 3 weeks. Blood and urine levels for promacetin, and skin and nasal scrapings were performed periodically.

Among patients treated with promin, diasone, and sulfetrone at this institution, it is routine practice to administer iron and vitamin therapy when there is only a slight drop in the erythrocyte count, since it is known that there is a tendency on the part of these drugs to produce anemia. In the promacetin group of patients, iron and vitamin therapy, as well as liver and gastric mucosal preparations, were withheld unless the patient presented an initial anemia or showed a persistent decrease in the erythrocyte count during treatment. Such a procedure was necessary in order to determine the actual effect of promacetin on the peripheral blood elements. Three patients inadvertently, however, were given blood boosting preparations during insignificant decreases in their erythrocyte counts which were well within the realm of laboratory variation.

This drug evaluation began on March 1, 1948, and data were collected for the purposes of this report up to July 31, 1949.

### **Toxicity and Other Complications**

Among this group of 27 patients there occurred no severe acute toxic symptoms. Eleven patients had minor complaints of a transitory character occurring either during the first few days of treatment or when the dose of promacetin was increased. Headache, lethargy, and drowsiness occurred in four patients; dizziness in three patients; anorexia and gastric distress in seven; and temporary tinnitus in one (table 2). Drug fever did not occur. None of the listed symptoms required suspension of treatment and interfered little, if any, with the regular administration of the drug. Sodium bicarbonate taken with the promacetin relieved anorexia and gastric distress.

In regard to chronic toxic manifestations all patients were closely

**Table 2. Minor transitory acute toxic symptoms occurring in 11 patients**

Symptoms	Number of patients	Percent	Symptoms	Number of patients	Percent
Headache.....	4	15	Anorexia and gastric distress.....	7	26
Dizziness.....	3	11	Tinnitus.....	1	4
Lethargy and drowsiness.....	4	15			

watched especially for anemia, dermatitis, and kidney and liver injury. There was no clinical or laboratory evidence of kidney or liver damage, or of dermatitis.

Initial erythrocyte counts performed prior to treatment with promacetin indicated the need for immediate antianemic therapy in six patients. Since antianemic therapy was begun and maintained, this eliminated any further consideration of these patients in respect to their erythrocytes except that it should be mentioned that their counts gradually rose to normal during active treatment with promacetin. Among two-thirds of the remaining patients (14 out of 21), a slight depression of erythrocyte counts was noted in the first 2 to 4 weeks of treatment. Antianemic therapy in the form of iron and vitamins was given to four of these patients, but withheld from the remainder. With but three exceptions, the patients who received no antianemic therapy returned as rapidly to their original level of erythrocytes as those who were given antianemic therapy. The clinical course of the disease in these three patients was altered by the development of lepra reactions associated with high fever. These reactions occurred approximately 3 months after inception of treatment, and at the time when a secondary rise in the erythrocyte level had begun. Two of these patients gave a history of similar lepra reactions with severe anemia prior to treatment, making it quite certain that these episodes in at least two of the patients were unrelated to the administration of promacetin. Erythrocyte counts of these patients returned to normal after the subsidence of the reactions with the administration of iron salts, vitamins, and liver extract. A summary of the erythrocyte count behavior follows with the symbol "AT" denoting the administration of antianemic therapy:

Decrease less than 0.5 million per cu. mm.....	5 patients (3 AT)
Decrease between 0.5 and 1.0 million per cu. mm.....	5 patients (1 AT)
Decrease between 1.0 and 1.5 million per cu. mm.....	4 patients (3 AT)
No change in erythrocytes.....	2 patients
Increase less than 0.5 million per cu. mm.....	4 patients
Increase between 0.5 and 1.0 million per cu. mm.....	1 patient

Leucopenia was not observed in any of the patients treated. Leucocytosis occurred with the same frequency as would be normally expected in moderately or far advanced leprosy. Mild erythema

nodosum occurred in 11 patients. Six of these patients had experienced such reactions prior to treatment with promacetin. Three patients developed lepra reactions during which there was a temporary exacerbation of specific leprous lesions. Two of these patients had experienced similar reactions prior to treatment with promacetin.

One patient who had had frequent previous attacks of iridocyclitis had repeated exacerbations of this condition. Pain from leprous neuritis, although not a common complaint in this group of patients, did persist in a mild form in some patients.

There were six patients altogether in whom treatment was discontinued, but in none of these could the reason for discontinuation of treatment be wholly attributable to promacetin. The reasons were as follows: refusal of patient to cooperate because of psychotic episode unrelated to the drug, 1; irregular discharges (two improved nodular cases, one showing no change), 3; and acute lepra reactions, 2.

### Therapeutic Effect

The evaluation of the therapeutic effect of promacetin on leprous skin and mucous membrane lesions was primarily confined to the 21 patients listed in table 1 as having clinically active lesions when treatment was begun. The patients are referred to as group I. Those patients, six in number, who presented clinically inactive or residual lesions are utilized mainly in this report for a demonstration of bacteriologic response. These patients are referred to as group II.

Group I patients were treated for periods varying from 4 to 16 months and received a total of 13,811 gm. of promacetin. The total amount for each patient averaged 658 gm. The total amount of the drug taken by each patient may be found in the summary of cases (table 3).

Early objective improvement in specific skin lesions, as well as in secondary infected skin ulcerations, occurred in all of these patients. The duration of treatment before objective clinical improvement could be detected by careful physical examination varied from 2 to 8 weeks. The earliest change noted was a change in color in the form of a fading or tanning of macules and of the diffusely infiltrated areas of skin. This change usually became evident after about 2 to 4 weeks of treatment. At the same time there was a decrease in the edema of the dermal tissues associated with softening of the skin over the areas of diffuse infiltration and a decrease in the turgidity of the nodules. Definite shrinking of the nodules and decrease in infiltration of the skin did not occur until after at least 1 to 2 months of treatment. Necrosis of nodules before actual decrease in size took place was observed in some patients. Necrosis was followed by ulceration and crusting which rapidly healed. If swelling of the hands and feet were present, this manifestation also responded early and readily.

Mucous membrane lesions of the nose, mouth, and throat showed the effects of early healing in relief obtained from nasal obstruction and hoarseness during the first few weeks of treatment. Objective evidence of healing was observed by the workers in the eye, ear, nose, and throat, and dental departments. The dental officer gave the opinion that promacetin accomplished the healing of active mucous membrane lesions of the mouth and throat more rapidly than that observed from other sulfones.

Objectively, clinical improvement was progressive throughout the interval of treatment except in one patient. This patient (No. 1959), whose major skin manifestation was a number of infiltrated lepromatous patches, showed initial improvement which was followed by a temporary outburst of many small erythematous patches. After these lesions subsided, another exacerbation of lesions occurred after 6 months of treatment over larger areas of the body associated with fever, hoarseness, and nasal obstruction typical of an acute lepra reaction. Promacetin was discontinued. After remaining in a reactive stage for about 4 months this patient improved slowly and the skin and mucous membrane became negative for leprosy bacilli. Although there was eventual improvement in this patient he is classified in the summary as in worse condition at the end of the treatment interval than he was when treatment was begun. Another patient (No. 1942) developed a severe lepra reaction during which there was a temporary increase in the diffuse infiltration associated with high fever, neuritis, and secondary anemia. Promacetin was discontinued because of a continued reaction state and a refractory type of secondary anemia.

Among the patients treated was a psychotic one (No. 1372) who for a period of about 10 months had a remission from the mental disturbance. This patient presented far advanced confluent nodular skin lesions with very heavy diffuse infiltration and, during the remission of the mental state, promacetin was given and taken orally without much difficulty. Improvements in the specific lesions were rapid. By the time the nodules had flattened there was an exacerbation of the mental condition and all medication was refused. Four months later there was a definite return of infiltration and nodulation.

The patient having leprosy of the tuberculoid type (No. 1953) improved markedly and rapidly. This improvement cannot be attributed to promacetin entirely as tuberculoid leprosy generally improves spontaneously. The rapidity with which the lesions regressed in this case, however, suggests an added factor.

Another observation of interest denoting clinical improvement in the skin of some patients was regrowth of hair after about 6 months of treatment. The regrowth was scanty but nevertheless present. It appeared in eyebrow regions where eyebrows had been absent

Table 3. Summary of cases

Patient No.	Age	Sex	Type of leprosy	Type of skin lesion	Initial smears		Duration of treatment (months)	Maximum daily dose (gm.)	Total amount of drug (gm.)	First skin improvement noted (Weeks)	Condition of skin end of treatment interval	Last smears		Final disposition
					Skin	Nasal						Skin	Nasal	
1920	31	M	L <sub>2</sub> N	N and DI	3+	4+	16	4.0	1,255	2	Marked improvement	1+	1+	Treatment continued.
1931	23	M	L <sub>3</sub> N	DI, M	4+	3+	14.5	4.0	1,054	8	do	2+	0	Do.
1932	25	F	L <sub>2</sub> N	DI, M	4+	2+	14.5	3.0	883	3	do	4+	0	Do.
1372	(?)	F	L <sub>3</sub> N	DI	4+	4+	12	3.0	441	6	do	4+	4+	Discontinued.
1964	35	F	L <sub>2</sub> N	DI	3+	3+	12	3.0	613	4	Moderate improvement	1+	0	Treatment continued.
1974	57	M	L <sub>2</sub> N	DI	4+	4+	11	4.0	776	4	do	2+	0	Do.
1966	55	M	L <sub>3</sub>	N and DI	4+	4+	12	4.0	1,090	4	Marked improvement	4+	1+	Do.
1960	38	M	L <sub>2</sub>	DI, M	3+	3+	11	4.0	1,053	4	do	4+	0	Do.
1956	42	M	L <sub>2</sub>	DI, M	4+	4+	7	3.0	253	4	Slight improvement	3+	(?)	Abandoned.
2010	38	M	L <sub>2</sub>	DI, M	4+	2+	4	3.0	256	3	do	3+	1+	Treatment continued.
1949	51	M	L <sub>2</sub>	DI, M	4+	4+	12.7	3.0	781	2	Moderate improvement	2+	1+	Do.
1993	35	M	L <sub>2</sub>	DI, M	4+	4+	6.5	2.0	300	2	Slight improvement	4+	2+	Do.
2009	65	F	L <sub>3</sub>	DI, M	3+	2+	4.3	1.5	175	5	do	4+	1+	Do.
1942	42	F	L <sub>2</sub>	N and DI	4+	3+	9	3.0	352	2	Moderate improvement	1+	0	Discontinued.
1959	60	M	L <sub>1</sub>	M	2+	0	10	4.0	768	4	Worse	0	0	Treatment continued.
1951	42	M	L <sub>1</sub>	M	2+	0	9	4.0	1,211	3	Marked improvement	3+	1+	Do.
1953	44	M	L <sub>1</sub>	Plaques	0	0	13.5	4.0	911	3	do	0	0	Do.
1955	15	M	L <sub>1</sub>	M	2+	1+	13	4.0	1,042	2	do	2+	0	Do.
1992	49	F	L <sub>3</sub>	N, DI, M	4+	4+	7	2.0	163	6	Moderate improvement	4+	0	Do.
2002	51	F	L <sub>1</sub>	M, DI	2+	2+	4.3	3.0	275	3	Slight improvement	1+	0	Do.
2012	25(?)	F	L <sub>1</sub>	M, DI	1+	2+	4.5	2.0	139	3	do	2+	0	Do.
1695	48	F	L <sub>3</sub>	Residual	4+	4+	16.5	3.5	924	4	Renewed clearing	1+	0	Do.
1947	46	M	L <sub>2</sub>	Residual	3+	0	3	1.5	118	1	No change	3+	0	Abandoned.
1759	30	F	L <sub>1</sub>	Residual	1+	0	14	1.0	113	1	do	1+	0	Treatment continued.
796	55	M	L <sub>3</sub>	Residual	4+	1+	15	1.0	276	0	Renewed clearing	2+	0	Do.
1902	38	M	L <sub>2</sub>	Residual	1+	0	13	3.0	728	0	do	1+	0	Do.
1957	31	F	L <sub>2</sub>	Residual	3+	1+	12	2.5	451	1	do	0	0	Do.

\*N—Nodules.

\*DI—Diffuse infiltration.

\*M—Infiltrated macules.

prior to treatment and on the extremities and chest. Subjective improvement in the sensation of the extremities took place in some patients.

Reduction in the number of leprosy bacilli in the skin did not become noticeable in skin smears until after 1 year's treatment. A few heavy nodular cases continued to show the same number of organisms in the skin smears although the absolute number of organisms must have been significantly reduced by the decrease in size of the lesions. The mucous membranes showed a reduction in bacilli at an earlier stage and many patients showed negative nasal smears at the end of 1 year's treatment.

Group II patients, presenting only residual lesions, were treated for periods varying from 3 to 15 months. They received a total of 2,613 gm. of promacetin or an average of 435 gm. per patient. Actual amounts given to each patient may be found in the summary of cases (table 3).

Table 4. *Clinical status of patients (group I) at end of treatment interval*

Treatment period	Clinical status				
	Marked improvement	Moderate improvement	Slight improvement	Worse	Total
Number patients treated 12 months or more.....	8	2	-----	-----	10
Number patients treated 6 months-12 months.....	1	3	2	1	7
Number patients treated 3 months-6 months.....	-----	-----	4	-----	4
Total.....	9 (43%)	5 (24%)	6 (28%)	1 (5%)	21

Group II patients were expected to show little if any change in their skin manifestations. Four of these patients surprisingly, however, began to show renewed clearing of their skin after 3 to 6 months' treatment. One patient left the hospital without permission after 3 months' treatment, and the sixth patient (No. 1759), because of repeated lepra reactions which she also had prior to promacetin treatment, received only interrupted treatment in small doses to the extent of 113 gm. in 14 months. These two patients showed no change

Table 5. *Bacteriologic status of patients at end of treatment interval*

Treatment period	Bacteriologic status					
	No change		Reduction in bacilli		Negative	
	Skin	Nasal	Skin	Nasal	Skin	Nasal
Number patients treated 12 months or more.....	4(1)	1	5(3)	3	(1)	4(2)
Number patients treated 6 months-12 months.....	4	1	2	0	1	3
Number patients treated 3 months-6 months.....	3(1)	0	1	2	0	2

Numbers in parentheses represent group II patients (residual lesions); plain numbers, group I. Discrepancy in number is accounted for by omission of those patients who had negative skin smears or nasal smears at beginning of treatment and remained negative.

in the skin, but the repeated lepra reaction experienced by one of them gradually abated.

There was a reduction in the number of leprosy bacilli in the skin of all of these patients who showed renewed clearing of the skin, and one became negative. While two had positive nasal smears at the inception of treatment, all of them had negative nasal smears at the end of the treatment interval.



Before treatment

Figure 1.  
Photographs showing  
response to treatment  
of extensive  
nodulation of skin.



5 months' treatment



12 months' treatment

The clinical condition of group I patients at the end of their treatment interval is classified in table 4. Status in regard to the bacterioscopic condition of skin and mucous membranes of both groups of patients is given in table 5.

Clinical photographs of representative cases serve further to illustrate the effect of promacetin on leprous lesions (figs. 1 and 2).

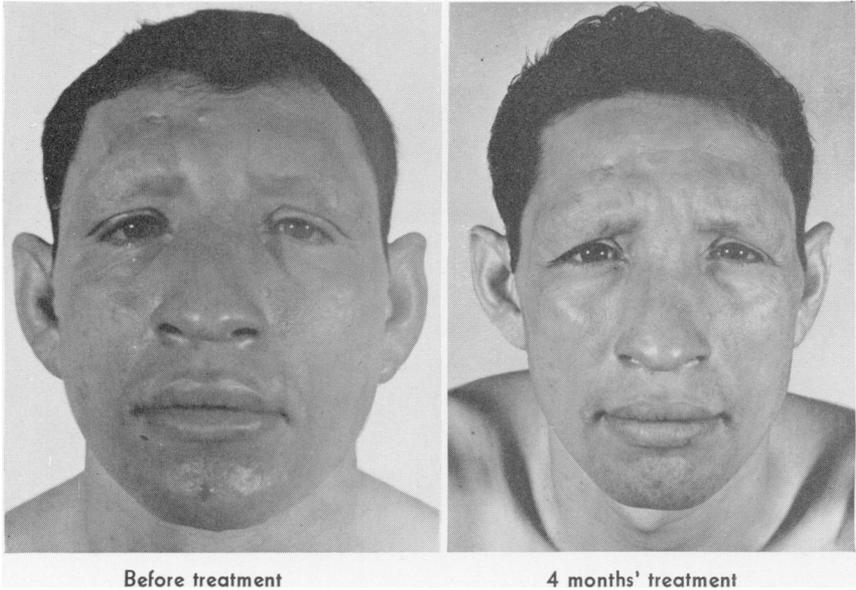


Figure 2. Photographs showing response to treatment of diffuse infiltration and small discrete nodules.

### Discussion

The final status of these 27 patients at the end of their individual treatment intervals was on the whole improved. Those who had no prior sulfone treatment, in addition to objective improvement, showed the usual subjective improvement manifested by an air of well being, increase in appetite and weight gain. Those who had long periods of treatment with sulfones prior to promacetin seemed to benefit by a change in treatment as shown by the renewed clearing of their skin and by the further reduction of leprosy bacilli in their specific lesions.

The early changes in macules and infiltrations observed following treatment might be looked upon by the experienced leprologist as possibly due to the spontaneous forces of natural regression aided by rest and hospital care. This is not believed to be a tenable explanation for the improvement in all patients. The change in the various lesions was remarkably uniform in time and appearance in all patients. It was sustained as long as promacetin was administered. With-

drawal of the drug was followed by a reappearance of lesions in due time. All of these considerations point to the drug administered as the causative agent for the improvement observed.

Early improvement in infected skin ulcerations suggests that promacetin, in addition to having antileprotic properties, is capable of combating secondary infections. Relief from nasal obstruction and dryness of the throat sustained by patients taking the drug also is evidence in favor of its ability to combat ordinary infections.

It was found in the determination of promacetin blood levels that the blood level remained fairly constant between 1.5 to 2.0 mg. per 100 cc. of blood on oral doses varying from 3.0 to 4.0 gm. daily irrespective of the length of treatment. Urine levels behaved differently. In the early weeks and months of treatment the urine level on the stated dosage averaged around 25 to 50 mg. per 100 cc. of urine. After 6 to 9 months of treatment the urine levels tended to increase going as high as 200 to 250 mg. per 100 cc. of urine. Eventually, some patients excreted by way of the kidneys almost as much of the drug daily as was administered. An adequate explanation for the increase observed in the urine promacetin level after prolonged treatment while there was very little increase in the blood level of the drug cannot be given at present. After prolonged treatment significant amounts of promacetin were excreted in the urine up to 12 days following discontinuation of the drug.

The opinion expressed by some that sulfones are of no value in tuberculoid leprosy is probably influenced by the feeling that this type of leprosy is not in need of treatment. The improvement noted in the patient of this type treated with promacetin was certainly more striking and rapid than that usually observed without treatment.

### Conclusions

Objective clinical improvement of skin and mucous membrane lesions of lepromatous leprosy is observed to occur following the oral administration of promacetin. The improvement noted is uniform, universal and sustained; therefore, it cannot be wholly attributed to spontaneous factors.

Reduction in the number of leprosy bacilli in the skin and mucous membrane follows clinical improvement. Skin smears commence to show a noticeable reduction of bacilli at the end of 1 year's treatment while many patients show an absence of bacilli in the mucous membrane at this time.

Promacetin is well tolerated orally even upon prolonged administration of doses as high as 3.0 to 4.0 gm. daily. Slight depression of the erythrocyte count may occur during the first few weeks of treatment. Unless there are other complications of the disease present, such depressed counts usually return to the original level spon-

taneously. Before it can be definitely stated that promacetin does or does not have the property of producing severe grades of anemia when used in the treatment of uncomplicated leprosy, further blood studies on a larger group of patients are necessary.

Renewed clearing after promacetin therapy of apparently stationary residual lesions in patients previously treated with sulfones suggests that a wider application should be made of alternating or combined methods of treatment in leprosy.

Promacetin apparently possesses chemotherapeutic properties against human leprosy. Its lack of protection against tuberculosis of guinea pigs and its apparent effectiveness in another acid fast infection, human leprosy, present interesting implications as to the future choice of experimental drugs for trial in both human leprosy and human tuberculosis.

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## EIGHT NEW *SALMONELLA* TYPES

The eight new *Salmonella* types described here were recognized during a survey of enteric infections in Hidalgo County, Texas. The reports on the new types are presented in combined form.

### *Salmonella edinburg* and *Salmonella san-juan*

By JAMES WATT,\* THELMA DeCAPITO,\* P. R. EDWARDS,\*\* and G. J. HERMANN\*\*

These two *Salmonella* types were isolated during the course of a study of enteric infections in Hidalgo County, Texas.

*Salmonella edinburg*. This type is represented by two cultures obtained by rectal swab from two children residing in Edinburg, Texas.

Two families, M. and F., were involved, and were studied with monthly records of illness and monthly stool culture examinations. Family M. consisted of the father, mother, and two children, one female, aged 3, and one male, aged 1. Family F. consisted of a mother and seven children.

The mother F. was employed by family M., and she and her children lived in a small house on the rear of the premises. There was close contact between all members of these family groups. The two families moved into the study area in May 1947. Cultures were taken from the two M. children and five youngest F. children at that time, and also in June. A few days after these cultures were taken, baby R. F., male, 1 month, became ill with a moderate diarrhea lasting about 10 days. He apparently recovered, but several days later he developed a high fever and died July 7. The diagnosis made by the family physician was pneumonia. Four days later, J. F., 3-year-old female, became ill with a diarrheal disorder. She had 10 to 15 liquid bowel movements a day, without gross blood or mucous. This diarrhea was accompanied by marked anorexia, fever, and abdominal pain. These symptoms persisted for approximately 10 days, and she was just recovering at the time of culture July 21, 1947. The stool culture was positive for *Salmonella edinburg*, both on direct plating with SS agar, and also from the tetrathionate enrichment broth plated to SS agar. No other members of the family gave a

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history of diarrheal disease at that time or during a 3-month follow-up period. Cultures were taken from four of the siblings at that time and during the next 3 months. No pathogens were isolated from any of these children from whom cultures were taken in August, September, and October.

Both children in family M. became ill at about the same time that J. F. became ill. R. M., 3-year-old female, had a moderate diarrhea with from five to eight liquid stools per day for 4 days. This was accompanied by anorexia, headache, and moderate amount of abdominal pain. Her brother, 1-year-old, became sick the next day with three to four liquid stools. There was no fever or abdominal pain. Both children had completely recovered by the time of the culture July 21, 1947. *Salmonella edinburg* was isolated by the enrichment technique from the stools of R. M. No pathogen was isolated from the culture of her brother. Both were cultured on three succeeding months and did not have any additional positive cultures.

Thus, from the four individuals giving a history of illness, *Salmonella edinburg* was isolated from two. A third was not cultured until after clinical recovery was complete, and the fourth, R. F., was ill and died without having a culture taken subsequent to the onset of illness. The symptomology recorded for his fatal illness is compatible with a diagnosis of salmonellosis, but cultural evidence for such a diagnosis was not obtained. Neither of the two families involved owned any domestic animals. However, there were a number in the immediate vicinity. Cultures were taken from most of these animals during the week of August 4, but no recovery of *Salmonella edinburg* was made. No evidence as to the original source was obtained.

The cultures possessed the usual biochemical pattern of the *Salmonella* group except that both liquefied gelatin after 14 days incubation at room temperature. Glucose, arabinose, xylose, maltose, trehalose, rhamnose, sorbitol, dulcitol, inositol, and mannitol were fermented with gas production within 24 hours. Cellobiose was fermented after 8 days. Lactose, sucrose and salicin were not fermented. The cultures utilized d-tartrate, l-tartrate, mucate, and citrate, but i-tartrate was not attacked. Hydrogen sulphide was produced but indol was not formed.

The cultures were agglutinated to the titer of *S. thompson* O serum (VI, VII) and in absorption tests removed all agglutinins from the serum. The H antigens were diphasic. Phase 1 was agglutinated by, and removed all agglutinins from, *S. paratyphi* B phase 1 serum (b). Phase 2 was agglutinated by serums for all the nonspecific phases. When tested with absorbed serums for single factors two, three, five, six, and seven, it was agglutinated only by serums for three and five. In absorption tests the organism left a slight residue of agglutinins for the homologous strain in *S. thompson* phase 2 serum (1,5).

However, it removed all agglutinins for phase 2 of *S. cholerae-suis* (1,5). The antigenic formula of *S. edinburg* is VI, VII: b-1, 5.

*Salmonella san-juan*. This organism is represented by two cultures obtained from domestic animals cultured as a part of the study of the epidemiology of salmonellosis. The type culture was isolated from a rooster in San Juan, Texas, August 25, 1947. Twenty-four other chickens were cultured on the same premises. No pathogens were isolated from these fowl. The second isolation was made August 28 from a cat in another town about 2 miles from San Juan. Cultures were taken from 17 other animals on those premises, including 10 chickens, 4 cows, 1 dog, and 1 other cat. No *Salmonellas* were isolated from the other domestic animals.

*S. san-juan*, like *S. edinburg*, slowly liquefied gelatin. One culture (cat) failed to ferment inositol. Otherwise the biochemical characteristics were the same as those of *S. edinburg*.

*S. san-juan* also belonged to the VI, VII group and removed all agglutinins from *S. thompson* O serum. The H antigens were diphasic and phase 1 was agglutinated to titer by *S. paratyphi* A serum (a). A marked residue of agglutinins for the homologous strain remained after absorption of *S. paratyphi* A serum by phase 1 of *S. san-juan*. However, the serum no longer agglutinated phase 1 of *S. durban*, whose A antigen is somewhat different from that of *S. paratyphi* A.

Phase 2 of *S. san-juan* was agglutinated by single factor serums three and five. In absorption tests it behaved in the same way as phase 2 of *S. edinburg*, failing to clear completely the agglutinins from serum for phase 2 of *S. thompson* but removing all agglutinins for phase 2 of *S. cholerae-suis*. The antigenic formula of *S. san-juan* is VI, VII:a-1,5.

### Summary

*S. edinburg* is represented by two strains, both isolated from man. The antigenic formula is VI, VII:b-1,5. *S. san-juan*, whose antigenic formula is VI, VII:a-1,5, was isolated first from a chicken and later from a cat.

## *Salmonella lomita* and *Salmonella riogrande*

By P. R. EDWARDS,\* ALICE B. MORAN,\* JAMES WATT,\*\* and THELMA DECAPITO\*\*

These *Salmonella* types were isolated in the laboratory of the Dysentery Control Project, Public Health Service, during the course

\*Department of Animal Pathology, Kentucky Agricultural Experiment Station, Lexington, Ky. \*\*Dysentery Control Project, Public Health Service, Pharr, Tex. The work reported here was done in part in connection with a project of the Kentucky Agricultural Experiment Station and is published by permission of the director. This portion of the work was supported by a research grant from the Public Health Service.

of a survey of enteric infections in Hidalgo County, Texas.

*Salmonella lomita*. This type is represented by two cultures, one (culture 91) isolated from a cloacal swab from an apparently normal hen, the other isolated from a rectal swab taken from an apparently normal cat (culture 150). Both cultures produced H<sub>2</sub>S, failed to form indol, and slowly liquefied gelatin. Jordan's tartrate and Simmon's citrate mediums were utilized. When tested by the method of Kauffmann and Burón (2), d-tartrate, mucate, and citrate were fermented but i-tartrate was not attacked. Culture 150 (cat) fermented l-tartrate while culture 91 did not utilize the substance. Acid and gas were formed within 24 hours from glucose, arabinose, xylose, rhamnose, maltose, trehalose, dulcitol, sorbitol, and mannitol. Cellobiose was fermented slowly. Lactose, sucrose, raffinose, inositol, and salicin were not fermented.

On serological examination the O antigens of the cultures were identified as VI,VII. Culture 91 was somewhat rough and the O antigens were atypical, but culture 150 removed all agglutinins from VI,VII serum in absorption tests.

The H antigens were diphasic and phase 1 was identified as e,h. Although the organisms were agglutinated to the titer of serum for phase 1 of *S. reading*, a slight residue of agglutinins for the homologous strain was left after absorption of the serum with *S. lomita*. When tested with absorbed serums for single factors 2, 3, 5, 6, and 7, the cultures were agglutinated only by serum for factor 5. When serum derived from phase 2 of *S. thompson* was absorbed by phase 2 of *S. lomita*, the titer was reduced from 10,000 to 200. The antigenic formula of *S. lomita* is VI,VII:e,h-1,5.

*Salmonella riogrande*. This type is represented by one culture isolated from a rectal swab culture of an apparently normal dog. The biochemical characteristics differ from those of *S. lomita* only in that inositol was fermented promptly and l-tartrate was not utilized. This type also liquefied gelatin.

The O antigens of *S. riogrande* were unlike those of any previously recognized *Salmonella* type and the organism was not agglutinated in significant dilution by any *Salmonella* O serum. When tested with serums for other groups of Enterobacteriaceae, it was agglutinated to the titer of serum for Arizona O antigen 10 (1). In absorption tests it left a slight residue of agglutinins for the homologous strain. Since this antigen has not appeared before in the genus *Salmonella*, it is assigned the symbol XL.

*S. riogrande* was diphasic and phase 1 was agglutinated to the titer of serum for phase 1 of *S. paratyphi* B (b). In absorption tests it reduced the titer of the serum from 10,000 to 500. Phase 2 was agglutinated by serums for all the nonspecific phases and by serum for single factor 5. In absorption tests it left a slight residue of

agglutinins for the homologous strain in serum for phase 2 of *S. thompson*. The antigenic formula of *S. riogrande* is XL:b-1,5.

### Summary

*S. lomita* (VI,VII:e,h-1,5) was represented by two cultures, one isolated from a cloacal swab from a normal hen, the other from a rectal swab taken from a normal cat. *S. riogrande* (XL:b-1,5) was isolated from a rectal swab from a normal dog. This type had O antigens unlike those of any previously recognized *Salmonella* but they were closely related to O antigen 10 of the Arizona group. Both types liquefied gelatin.

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- (2) Kauffmann, F. and Alonso Burón, F. Kulturelle Untersuchungen in der *Salmonella*-Gruppe mit besonderer Berücksichtigung der organischen Säuren. *Ztschr. f. Hyg. u. Infektionskr.* 117: 650-661 (1935).

## **Salmonella weslaco and Salmonella macallen**

By P. R. EDWARDS,\* G. J. HERMANN,\* JAMES WATT,\*\* and THELMA DECAPITO\*\*

An organism isolated in 1947 in the laboratories of the Dysentery Control Project from the rectal swab of a normal cat seemed upon preliminary examination to possess the biochemical properties characteristic of *Salmonella*. Later it was found that the culture slowly liquefied gelatin. Upon serological examination, it was found that the O and H antigens of the culture could be expressed by symbols applied to the Arizona group of paracolón bacteria by Edwards, West and Bruner (1). The antigenic formula of the culture was Ar. 15:17, 20. The culture differed from typical Arizona strains in that it utilized d- and l-tartrate, fermented dulcitol, and did not attack lactose. The culture remained undescribed since it was impossible to orient its antigens in the Kauffmann-White classification. Later two additional cultures of the same type were isolated, one from a rectal swab of a normal dog, and a second culture from an apparently healthy cat.

In 1948 the personnel of the Dysentery Control Project isolated three cultures which had *Salmonella* O antigens III, X and which possessed H antigens closely related to those of the strains previously isolated. These group E cultures were isolated from rectal swabs taken

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from two dogs and a cat. All the animals lived in the same vicinity, and all were apparently healthy. The relationship of these cultures to group E of the Kauffmann-White classification made it possible to orient all cultures in the genus *Salmonella*.

The first mentioned cultures, represented by the Arizona formula 15:17,20, were called *Salmonella weslaco* since the first culture was isolated in Weslaco, Texas. The cultures produced hydrogen sulfide but did not form indol. Acid and gas were formed in 24 hours from glucose, arabinose, xylose, rhamnose, maltose, trehalose, dulcitol, sorbitol, and mannitol. Cellobiose was acidified after 5 days. Lactose, sucrose, raffinose, inositol, and salicin were not fermented. Vigorous growth occurred on Simmons' citrate agar, and acid was produced in Jordan's tartrate agar. When tested by the method of Kauffmann and Burón (2) the organism completely utilized d-tartrate, mucate, and citrate, but did not attack i-tartrate. Two cultures utilized l-tartrate; the third did not.

As mentioned, the O and H antigens were related to those of Arizona 15:17,20. The O antigens of *S. weslaco* were identical with those of Pc 139 (Ar. 015) as shown by reciprocal absorption tests. Since these antigens were unrelated to any previously reported in *Salmonella* strains, they were assigned the symbol XLII. The H antigens of *S. weslaco* were agglutinated by single factor serums for Arizona H factors 17 and 20. Cross agglutination to the titer of the H serums occurred between *S. weslaco* and Pc 107 (Ar. 17,20). In reciprocal absorption tests each organism reduced the titer of serum derived from the other by 50 percent. The H antigens of *S. weslaco* were assigned the symbol z<sub>36</sub>. Thus, it is represented by the formula XLII:z<sub>36</sub>.

The group E strains were isolated in McAllen, Texas, and were called *Salmonella macallen*. Like *S. weslaco*, *S. macallen* slowly liquefied gelatin. The biochemical characteristics of *S. macallen* differed from those of *S. weslaco* only in that the former promptly fermented inositol. *S. macallen* also gave variable results in l-tartrate. The O antigens of *S. macallen* were closely related to those of *S. anatum*, and each was agglutinated to the titer of serum derived from the other. In absorption tests a slight residue was left in each serum, indicating that the two were not identical. However, *S. macallen* removed all agglutinins for *S. newington* and *S. senftenberg* from *S. anatum* O serum. Like *S. weslaco*, the H antigen of *S. macallen* was agglutinated strongly by Pc 107. The identity of the H antigens of *S. macallen* and Pc 107 was demonstrated by reciprocal absorption tests. The relations of the H antigens of *S. macallen* to those of *S. weslaco* were the same as the relations of the latter to the H antigens of Pc 107. Since the H antigens of *S. macallen* were similar to those of *S. weslaco*, and since for diagnostic purposes it was not necessary

to differentiate between them, *S. macallen* was also assigned the symbol z<sub>36</sub>. The antigenic formula of *S. macallen* is III, X:z<sub>36</sub>.

*S. weslaco* is not the first *Salmonella* type which could not be oriented in the Kauffmann-White schema when first isolated. *S. cerro* had no serological relations to known *Salmonella* types and was excluded from the schema until *S. düsseldorf* was recognized. It is of particular interest that *S. cerro* also has close O and H relationships to the Arizona paracolon bacteria. These circumstances emphasize the fact that an antigen should not be referred to as a "salmonella antigen" or a "paracolon antigen." The continuity of antigens among the Enterobacteriaceae is so pronounced that it is not always possible unequivocally to assign an organism to a certain genus. As larger numbers of cultures are studied it becomes increasingly apparent that the family is composed of a series of strains with related and interlocking antigens and that in many instances their classification in a given genus is a purely arbitrary matter which should be settled by international agreement.

### Summary

Two new *Salmonella* types, *S. weslaco* (XLII:z<sub>36</sub>) and *S. macallen* (III,X:z<sub>36</sub>) were isolated from cats and dogs. Each type was represented by three cultures. The organisms were serologically related to the Arizona group of paracolon bacteria. The continuity of antigens in the Enterobacteriaceae and the difficulty of assigning certain cultures to a given genus were mentioned.

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## *Salmonella donna* and *Salmonella pharr*

By JAMES WATT,\* THELMA DECAPITO,\* G. J. HERMANN,\*\* and P. R. EDWARDS\*\*

*Salmonella donna*. This type was represented by two cultures isolated from rectal swabs, one from a normal baby and one from an apparently healthy cat. The biochemical properties of the cultures were those generally attributed to *Salmonella* except that gelatin was slowly liquefied. Acid and gas were produced in 24 hours from glucose, arabinose, xylose, rhamnose, maltose, trehalose, culcitol,

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sorbitol, mannitol, and inositol. Cellobiose was acidified after 6 days. Lactose, sucrose, raffinose and salicin were not fermented. Hydrogen sulfide was formed but indol was not produced. Vigorous growth occurred on Simmons' citrate agar, and acid was produced in Jordan's tartrate agar. When tested by the method of Kauffmann and Burón (1), the organisms completely utilized d-tartrate, citrate and mucate but l- and i-tartrate were not fermented.

On serological examination the organisms were agglutinated to the titer of *S. urbana* O serum (XXX). In absorption tests the organisms were unable to exhaust the serum of agglutinins, a residue of 25 percent of the titer remained after absorption. The O antigens of *S. donna* may be represented by the symbol XXX. The H antigens were diphasic and phase 1 was agglutinated in high dilution by serums containing agglutinins for antigens 1,v;1,w;1,z<sub>13</sub> and 1,z<sub>28</sub>. When tested with single-factor serums the organisms were agglutinated by v serum but not by w,z<sub>13</sub> or z<sub>28</sub> serums. In absorption tests, all H agglutinins were absorbed from 1,v serum derived from *S. bredeney*.

Phase 2 of *S. donna* was agglutinated by serums for all the non-specific phases. When tested with absorbed single factor serums, it reacted with serum for factor 5 but not with serums for 2, 3, 6, or 7. In absorption tests, it reduced the titer of serum derived from *S. cholerae-suis* var. *kunzendorf* from 1 to 10,000 to 1 to 500. *S. donna* is represented by the antigenic formula XXX:1,v-1,5.

*Salmonella pharr*. This type was represented by one culture isolated from a rectal swab taken from a normal cat. The biochemical properties of *S. pharr* differed from those of *S. donna* only in that *S. pharr* failed to ferment maltose and utilized l-tartrate. This type also slowly liquefied gelatin.

*S. pharr* was agglutinated by O serum derived from *S. aberdeen*, and in absorption tests removed all agglutinins from the serum. The O antigens of the organism are XI. The H antigens were diphasic and phase 1 was agglutinated in high dilution by serum derived from phase 1 of *S. paratyphi B* (b). In absorption tests the titer of *S. paratyphi B* serum was reduced from 1 to 10,000 to 1 to 1000 by absorption with phase 1 of *S. pharr*. For diagnostic purposes phase 1 may be denoted by the symbol b.

Phase 2 was agglutinated by e,n,x and e,n,z<sub>15</sub> serums. When tested with single-factor serums for x,z<sub>15</sub>, z<sub>16</sub> and z<sub>17</sub> it reacted with z<sub>15</sub> and z<sub>17</sub> serums. In absorption tests, phase 2 of *S. pharr* left a pronounced residue of agglutinins in e,n,z<sub>15</sub> serum for both e,n,x and e,n,z<sub>15</sub> forms. It can be concluded only that the phase lacks a portion of the antigenic complex denoted by the symbol n. For diagnostic purposes, phase 2 of the culture may be represented by the symbols e,n,z<sub>15</sub>. The antigenic formula of *S. pharr* is XI:b-e,n,z<sub>15</sub>.

## New Types Found in Hidalgo County

During the 2 years in which studies on the effect of fly control on diarrheal diseases were conducted in Hidalgo County, Texas, 11 new *Salmonella* types were recognized. A total of 43 different types were found in men and animals; thus, a quarter of the types identified were first isolations. Of the new types, 7 were isolated from animals, 2 from man, and 2 from both man and animals.

The table lists these new types and presents some interesting points of similarity. Ten of the 11 types possessed a characteristic uncommon in the *Salmonella* group—the liquefaction of gelatin. Six of the types possessed similar but not identical phase-2 antigenic structures, and 3 others, similar but not identical phase-2 antigenic complexes. *S. macallen* and *S. weslaco* appear closely related in that they share similar H antigens which are also found in the Arizona group of paracolon bacilli. The explanation of these similarities is not certain. The fact that so many new types were found in a relatively small geographical area and that these types appear to be closely inter-related is compatible with the theory that the presently recognized *Salmonella* types are descended from more complex ancestors.

*New Salmonella types isolated in Hidalgo County, Tex.*

Type	Antigenic formula			Gelatin liquefaction
	"O"	Phase 1	Phase 2	
<i>S. texas</i> .....	IV, V, XII	k	enz <sub>15</sub>	+
<i>S. hidalgo</i> .....	VI, VIII	r	enz <sub>15</sub>	-
<i>S. pharr</i> .....	XI	b	enz <sub>15</sub>	+
<i>S. riogrande</i> .....	XL	b	1, 5	+
<i>S. edinburg</i> .....	VI, VII	b	1, 5	+
<i>S. san-juan</i> .....	VI, VII	a	1, 5	+
<i>S. mission</i> .....	VI, VII	d	1, 5	+
<i>S. lomita</i> .....	VI, VII	eh	1, 5	+
<i>S. donna</i> .....	XXX	1v	1, 5	+
<i>S. macallen</i> .....	III, X	z <sub>36</sub>	-----	+
<i>S. weslaco</i> .....	XLII	z <sub>36</sub>	-----	+

### Summary

Two new *Salmonella* types, *S. donna* (XXX:1,v-1,5) and *S. pharr* (XI:b-c,n,z<sub>15</sub>) are described. *S. donna*, represented by two cultures, was isolated from a child and a cat. *S. pharr*, represented by one culture, was isolated from a normal cat. The 11 new types of *Salmonella* isolated in a single county in Texas are summarized and the antigenic similarities noted.

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# Factors Affecting Hospital Construction In High Priority Areas

By LOUIS S. REED, PH. D., HELEN HOLLINGSWORTH, A. B.,  
and ANNA MAE BANEY, A. B.\*

The primary purpose of the hospital survey and construction program is to construct hospitals and public health centers in areas of the greatest need, giving special consideration to both rural communities and those with relatively small financial resources. Although the program thus far has been quite successful in building needed facilities in many such areas, this objective has not been attained in full. Studies of the distribution of approved general hospital projects according to area priority indicate that, although 58 percent of all general hospital projects financed from 1948 allotments and 43 percent of all such projects financed from 1949 allotments are in "A" priority areas, more than 20 percent of the projects in 1948 and 30 percent in 1949 are in areas of "C" or lower priority rating. An analysis of the general hospital service areas with and without projects indicates that a somewhat greater proportion of the high rather than the very low per capita income areas are submitting projects. Similarly a larger proportion of base than of rural areas have projects.

In order to determine the major reasons why high priority areas without projects have not submitted applications for hospital construction, this special study has been made in cooperation with the State agencies.

During the latter part of February and March, data were obtained from all but three States—Delaware, New York, and Pennsylvania.<sup>1</sup> In the majority of States, an area frequently included more than one community. The reason given for failure to submit project applications in many areas differed for the individual communities within an area. Therefore, the following analysis has been based on the reasons reported for the separate communities rather than for a complete area. In the entire study, these reasons were provided for 436 communities in 396 "A" priority areas and 261 communities in 192 "B" priority areas.

Of the 436 communities in "A" areas, 129 have either just recently completed a project or have one scheduled or under way with or without Federal aid. Included among these 129 communities are those in which a fund drive is in process and those in which a project has

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<sup>1</sup> Nevada is also excluded since, as of that date, Nevada had not submitted a plan for hospital construction.

been scheduled for a later year. For the remaining 307 "A" priority communities having no hospital project planned or scheduled, a total of 414 reasons was given for the lack of a project; more than one reason was given for some communities.

The area's lack of financial ability to construct and/or maintain a hospital was the leading reason given in 132 cases, 32 percent of the total. It is significant that the per capita income of virtually all of these communities or hospital service areas is less than the State average; 5 percent have per capita incomes of less than one-third of the State average, 41 percent have per capita incomes of between one-third and two-thirds of the State average, and 38 percent have per capita incomes of between two-thirds and 100 percent of the State average. Only 7 percent of the communities have per capita incomes equal to or higher than the State average. Per capita income data were not available for the remaining areas—those in the Territories—which constituted 9 percent of the total. The per capita income represents the net effective income—disposable income or income after tax payments—for the year 1946 taken or derived from Sales Management.

The reason ranking second highest among those given for the lack of a project was lack of community interest and/or leadership. This reason was given in 101 instances—24 percent of the total. It is felt that there is a definite relationship between this lack of interest or leadership and the lack of ability to finance the construction and/or maintenance of a hospital. Many communities feel that they definitely cannot raise sufficient funds to finance a project so there is no community interest at all. Theirs is the feeling of "Why attempt the impossible?" This feeling, reflected in some of the reports, is borne out by the fact that the majority of these areas or communities are relatively poor—46 percent of them have per capita incomes of less than two-thirds of the State average and 49 percent, between two-thirds and 100 percent of the State average.

The availability of hospital service in the same or a nearby community led 59 communities, 14 percent of the total, to feel that there was no need for a facility. In some instances the available facility was one which the State agency had declared nonacceptable on the basis of fire or health hazards, obsolete construction, etc., but which the people of the community still considered a usable and suitable facility. In a few cases, the reply indicated that the area was improperly delineated and should not have been set up as a separate area. Lack of medical and/or hospital personnel constituted 4 percent of the total reasons given as to why applications for hospital construction had not been submitted.

Other reasons given for the lack of a project in these "A" priority communities vary widely. Among those cited are: opposition of

**Table 1. Reasons why high priority communities have not submitted applications for hospital construction, as of March 1949**

Item	"A" priority communities		"B" priority communities	
	Number	Percent	Number	Percent
Number of communities reporting, U. S. and Territories.....	436	100.0	261	100.0
Communities with projects completed, in process, or planned.....	129	29.6	89	34.1
With Federal aid <sup>1</sup> .....	84	65.1	56	62.9
Without Federal aid.....	42	32.6	27	30.3
Federal participation unknown.....	3	2.3	6	6.8
Total communities without projects scheduled or planned.....	307	70.4	172	65.9
Number of reasons given for lack of projects.....	414	100.0	212	100.0
Lack of financial ability to construct and/or maintain a facility.....	132	31.9	45	21.2
Distribution of communities by index of State per capita income:				
Less than 33½%.....	7	5.3	1	2.2
33½-66¼%.....	54	40.9	14	31.1
66¼-100%.....	50	37.9	20	44.5
More than 100%.....	9	6.8	8	17.8
Territories <sup>2</sup> .....	12	9.1	2	4.4
Lack of community interest and/or leadership.....	101	24.4	64	30.2
Distribution of communities by index of State per capita income:				
Less than 33½%.....	4	4.0	1	1.6
33½-66¼%.....	43	42.5	27	42.2
66¼-100%.....	49	48.5	28	43.7
More than 100%.....	3	3.0	8	12.5
Territories <sup>2</sup> .....	2	2.0		
Availability of service in same or nearby community.....	59	14.3	44	20.8
Lack of medical and/or hospital personnel.....	15	3.6	1	.5
Other <sup>3</sup> .....	85	20.5	38	17.9
Unknown <sup>4</sup> .....	22	5.3	20	9.4

<sup>1</sup> Includes projects for which fund drive is in process and those scheduled for a later year because of present financial or other difficulties.

<sup>2</sup> Per capita income data not available.

<sup>3</sup> Includes such reasons as opposition of professional groups, improper area delineation, legal problems, lack of sponsor, political conflict, etc.

<sup>4</sup> Includes such reports as "no plan to build", "no activity to date," etc.

medical professional groups; lack of sponsor; differences of opinion among the people of the area as to which of two or more communities in the hospital service area should have the hospital; political conflicts; legal difficulties such as a ceiling imposed by State law on county bond issues and conflicts as to method of financing a facility.

In 5 percent of the total, the reason for the lack of a project was unknown. Included among these are such reports as "no plan to build," "no activity to date," etc.

Substantially the same pattern applies to "B" priority communities without hospital projects. Of the 261 such communities 89, or 34 percent, have either just recently completed a project or have one scheduled or under way, with or without Federal assistance. For the remaining 172 areas or communities, 212 reasons were given to explain the lack of a project. The most frequent reason given was a lack of community interest and/or leadership, 30.2 percent. Of the communities for which this explanation was advanced, 44 percent had

Table 2. Reasons why "A" priority communities have not submitted applications for hospital construction, as of March 1949

State	Total communities reporting	Federally-aided projects scheduled or planned	Hospital construction completed, in process, or planned without Federal aid	Construction planned, use of Federal funds unknown from data reported	Lack of financial ability to construct and/or maintain a facility				Lack of community interest and/or leadership (includes communities needing community education)				Availability of hospital service in same or nearby community	Lack of medical and/or hospital personnel	Other <sup>3</sup>	Unknown <sup>4</sup>		
					Per capita income—Percent of State average				Per capita income—Percent of State average									
					All	Less than 33 1/4% 33 1/4%	66 2/3% 100%	Over 100%	All	Less than 33 1/4% 33 1/4%	66 2/3% 100%	Over 100%						
Totals, United States and Territories.....	436	84	42	3	\$ 132	7	54	50	9	£ 101	4	43	49	3	59	15	85	22
Alabama.....	24	68	1			5	4	1			8	5	1	2	5		2	
Arizona.....	2	1	1			7			1		1				1		2	1
Arkansas.....	6	4				1					3	1	2		1		2	
California.....	9	2	2			1												
Colorado.....	7	2				1												
Connecticut.....	3	2	1															
Delaware.....	( <sup>1</sup> )																	
District of Columbia.....	( <sup>2</sup> )																	
Florida.....	5	1				4	1	3			1	1			1			1
Georgia.....	10	65	3			1	1				1	1			1		2	
Illinois.....	3		1			2					1	1			3		4	
Indiana.....	13	6	1			2	1				1	1			3		1	
Iowa.....	9	5				4	2	2			1	1					4	
Kansas.....	( <sup>10</sup> )																1	
Kentucky.....	34	3	1			7	3	1			11	2	7	2	2	1	16	1
Louisiana.....	11	1	3			6	5	1			2	2	2	2	2		1	
Maine.....	6	1				2	3	3			3	3	3	3	1			
Maryland.....	2	2				2			2									
Massachusetts.....	5	2				2					2	2	2	2	2		9	
Michigan.....	19	2	1			4	1	4			6	6	6	6	1		4	
Minnesota.....	12	1				1	1				6	1	1	1	4		3	
Mississippi.....	15	3	4			4	1	1			2	2	1	1	5		1	
Missouri.....	11	1	2			3	3				1	1	1	1	4		4	
Montana.....	( <sup>11</sup> )																	
Nebraska.....	10		1			1		1			5		5	3	3		2	
Nevada.....	( <sup>12</sup> )																	
New Hampshire.....	4	1	13			2	2				2	2	2	1	1			
New Jersey.....	3	2				1					1							
New Mexico.....	10		15			2	2				1		1				1	



Table 3. Reasons<sup>1</sup> why "B" priority communities have not submitted applications for hospital construction, as of March 1949

State	Total communities reporting	Federally-aided projects scheduled or planned <sup>2</sup>	Hospital construction completed, in process, or planned without Federal aid	Construction planned, use of Federal funds from data reported	Lack of financial ability to construct and/or maintain a facility			Lack of community interest and/or leadership (includes community education)				Availability of hospital service in same or nearby community	Lack of medical and/or hospital personnel	Other <sup>3</sup>	Unknown <sup>4</sup>		
					Per capita income—Percent of State average			Per capita income—Percent of State average									
					All	Less than 33 1/3%	33 1/3%—66 2/3%	Over 100%	All	Less than 33 1/3%	33 1/3%—66 2/3%					Over 100%	
Totals, United States and Territories	261	56	27	6	5	14	20	8	64	1	27	28	8	44	1	38	20
Alabama	13	6 <sup>5</sup>				3	1	1	2		1	1		2		1	3
Arizona	5	1				1	1	1	4				4			3	
Arkansas	12	1	2	1	(7)				4		1	4		2		6	
California	7					3		1	1		1		1	1			
Colorado	6		2														
Connecticut	(8)																
Delaware	(8)																
District of Columbia	(10)																
Florida	11	2				3	1	2	4			4					
Georgia	21	6 <sup>8</sup>	12			2		2									
Iaho	2																
Illinois	(8)																
Indiana	(8)																
Iowa	(8)																
Kansas	1	1															
Kentucky	16	3	1			1	1		9		1	6		6		3	14
Louisiana	15					7	4	2	4		3	1				2	
Maine	9	2	1			2	1	1	6		4	2		6			
Maryland	(14)																
Massachusetts	(9)	3	1			2	2	2	1		1	1		1		2	
Michigan	10																
Minnesota	(8)																
Mississippi	2																
Missouri	12	4	3			1	1		1		1			2		2	
Montana	(16)																
Nebraska	13	1	2						2		1	1		3			
Nevada	(17)																
New Hampshire	4		18			1											
New Jersey	9	5				2		2	1		1			2		2	2
New Mexico	3		1			1	1		1		1			2		2	
New York	(9)																
North Carolina	3	3															
North Dakota	5	1	1						2		2			1		1	
Ohio	3	2							1		1						
Oklahoma	9		1			2		2	4		3	1					19



per capita incomes of less than two-thirds of the State average and 44 percent had per capita incomes of two-thirds to 100 percent of the State average.

The next most frequent reason advanced was lack of financial ability to construct and/or maintain a hospital; this reason was given in 21.2 percent of the cases. As with "A" priority areas, the per capita income of these areas was relatively low in comparison to the State average.

Availability of service in the same or nearby community was cited as an explanation for lack of a project in 20.8 percent of the areas; lack of medical and/or hospital personnel in 0.5 percent of the cases, and miscellaneous other reasons in 17.9 percent. For 9 percent of the areas no reason was advanced.

The tables show by State the number of "A" and "B" priority communities for which data were obtained and summarize the reasons given for the lack of hospital projects in these communities.

### Summary

The two most important reasons why communities in high priority areas thus far without hospital construction projects have not submitted projects are lack of financial ability to construct and/or maintain a hospital and lack of community interest or leadership.

# INCIDENCE OF DISEASE

*No health department, State or local, can effectively prevent or control disease without knowledge of when, where, and under what conditions cases are occurring*

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## UNITED STATES

### REPORTS FROM STATES FOR WEEK ENDED JANUARY 28, 1950

In the United States increases for the current week are noted in reported cases of diphtheria (from 149 to 199), influenza (from 4,563 to 6,512), measles (from 4,329 to 4,580), scarlet fever (from 1,649 to 1,860), typhoid and paratyphoid fever (from 43 to 50), and whooping cough (from 2,192 to 2,888).

The reported incidence of influenza increased in the South Atlantic, the East South Central, and the West South Central Divisions. The largest increases were in Georgia (314 to 1,400) and Virginia (558 to 1,173) in the South Atlantic Division. Other States reporting increases in influenza were: Kentucky (0 to 18), Tennessee (26 to 117), Alabama (98 to 287), and California (8 to 39). Hawaii reported 133 cases for the week. For the Nation, the 5-year (1945-49) median is 4,534 for the corresponding week. The cumulative total for reported incidence of influenza for the calendar year is 19,477, as compared with 17,341 for the corresponding 5-year (1945-49) median. However, on the basis of seasonal years, the current cumulative total of 50,007 cases is lower than the corresponding median of 53,611 for the 5 (1944-45 to 1948-49) years.

Reported incidence of whooping cough increased in all geographic divisions except the Pacific. These increases were mainly along the Atlantic Coast with the largest increase in Georgia (4 to 216). Other increases are noted in Vermont (27 to 92) and New York (241 to 300).

States reporting the largest increase in measles were Michigan (910 to 1,060) and California (118 to 266).

New Mexico reported 1 case of confirmed bubonic plague (glandular) in Maljamar, Lea County. One case of smallpox and an increase from 7 to 48 cases of scarlet fever were reported in Arizona. One case of anthrax was reported in New York.

For the Nation, meningococcal meningitis decreased from 106 to 79, pneumonia from 2,274 to 2,104, poliomyelitis from 117 to 114, and tularemia from 32 to 25.

Of 42 States and the District of Columbia reporting on rabies in animals, for 24 and the District of Columbia, there were no cases. The remaining 18 States reported 142 cases with the largest numbers in Texas (32), Kentucky (26), New York (17), and Georgia (14).

*Telegraphic case reports from State health officers for week ended January 28, 1950*

(Leaders indicate that no cases were reported)

Division and State	Diphtheria	Encephalitis	Influenza	Measles	Meningitis, meningococcal	Pneumonia	Polio-myelitis	Rocky Mountain spotted fever	Scarlet fever	Small-pox	Tularemia	Typhoid and paratyphoid fever	Whooping cough	Rabies in animals
<b>NEW ENGLAND</b>														
Maine.....	1			28	1	2			8				35	
New Hampshire.....	2			3		8			3				1	
Vermont.....									7				92	
Massachusetts.....	7			62		2			123				147	
Rhode Island.....									6				11	
Connecticut.....				18	1	59			16				121	
<b>MIDDLE ATLANTIC</b>														
New York.....	9	2	13	321	3	231	4		2146				300	17
New Jersey.....		1		416	1	73	1		47				189	1
Pennsylvania.....	10			108	2	65	2		114				245	
<b>EAST NORTH CENTRAL</b>														
Ohio.....	14		5	136	7	71	5		288			4	175	5
Indiana.....	8	1	4	66	1	1	1		53			2	31	
Illinois.....	2	1	1	94	6	69	2		78				67	3
Michigan.....				1,060	5	24	4		166		2	1	260	4
Wisconsin.....	2		11	157	3	15	2		68				162	
<b>WEST NORTH CENTRAL</b>														
Minnesota.....	1			36	2		5		33				17	
Iowa.....	1			185	1	1	5		10				9	6
Missouri.....	1		6	11	2	24			19			2	37	
North Dakota.....	1		1	2	4						5	5		
South Dakota.....				5		1	1		4				2	
Nebraska.....				97		1	1						9	
Kansas.....	1			43		20			39				9	3
<b>SOUTH ATLANTIC</b>														
Delaware.....			1	30					6				2	
Maryland.....	13		2	22	1	36	1		28		2	1	72	
District of Columbia.....				31					10				1	1
Virginia.....	4		1,173	40	1	132			35		1		33	
West Virginia.....			26	213	2	7			33				42	4
North Carolina.....	12			158			1		48		2		35	
South Carolina.....	7	1	26	138	3	16			2			1	10	6
Georgia.....	1		1,400	24	1	23	1		20		1		216	14
Florida.....	5		4	41	3	10	3		8				15	

EAST SOUTH CENTRAL										
Kentucky.....	8	18	9	1	9	28	2	1	18	26
Tennessee.....	8	117	84	4	32	32	2	2	48	6
Alabama.....	19	287	52	2	92	10	2	5	6	3
Mississippi.....	5	11	54	2	7	7	2	1	6	3
WEST SOUTH CENTRAL										
Arkansas.....	5	176	19	4	77	4	3	2	80	2
Louisiana.....	2	2	4	1	38	1	1	4	2	3
Oklahoma.....	5	135	5	1	79	52	34	1	8	24
Texas.....	26	2,831	93	10	646	52	3	3	135	32
MOUNTAIN										
Montana.....	1	15	38	13	33	33	1	1	3	3
Idaho.....	3	22	2	4	7	7	2	2	10	2
Wyoming.....	3	51	135	1	29	7	3	8	20	3
Colorado.....	3	12	12	45	10	10	1	1	14	3
New Mexico.....	1	124	74	18	48	48	1	1	26	16
Arizona.....	1	6	140	3	4	4	5	4	16	1
Utah.....	1	1	1	10	10	41	1	1	22	1
Nevada.....	1	6	27	5	24	17	18	14	14	1
PACIFIC										
Washington.....	1	6	27	5	24	17	18	14	14	1
Oregon.....	8	39	266	1	53	110	1	1	105	1
California.....	1	1	1	1	1	1	1	1	1	1
Total.....	199	10,652	4,580	79	2,104	114	114	114	1,860	50
Median, 1945-49.....	289	4,534	6,712	86	48	2,964	48	48	2,964	40
Year to date 4 weeks.....	719	19,477	16,869	352	8,850	478	4	4	6,166	108
Median, 1945-49.....	1,277	17,341	20,285	350	210	1	1	1	10,174	133
Seasonal low week ends.....	(27th July 9)	(30th July 30)	(35th Sept. 3)	(37th Sept. 17)	(11th Mar. 19)	(32d Aug. 13)	(35th Sept. 3)	(11th Mar. 19)	(39th Oct. 1)	(11th Mar. 19)
Since seasonal low week.....	4,900	50,007	36,029	1,265	3,41,960	22,605	13	13	3,312	30,435
Median, 1944-45 to 1948-49.....	8,843	53,611	46,409	1,316	19,156	36,374	71	71	3,694	33,354

<sup>1</sup> New York City only.

<sup>2</sup> Including cases reported as streptococcal sore throat.

<sup>3</sup> Delayed reports: New Jersey, 1 case of rabies in animals, week ended January 21; Michigan, 3 cases of poliomyelitis for 1949, not assignable to specific weeks.

*Andrax*: New York, 1 case.

*Baoboric plague*: One case in Maljamar, Lea county, New Mexico.

Alaska: Measles 30.

Hawaii: Influenza 133, scarlet fever 4.

## BUBONIC PLAGUE IN LEA COUNTY, NEW MEXICO

One case of bubonic plague (glandular) was reported and confirmed in Maljamar, Lea County, New Mexico, on January 27, 1950.

### DEATHS DURING WEEK ENDED JANUARY 28, 1950

	Week ended Jan. 28, 1950	Corresponding week, 1949
Data for 94 large cities of the United States:		
Total deaths.....	9,854	9,518
Median for 3 prior years.....	9,664	-----
Total deaths, first 4 weeks of year.....	39,042	40,114
Deaths under 1 year of age.....	670	635
Median for 3 prior years.....	680	-----
Deaths under 1 year of age, first 4 weeks of year.....	2,527	2,745
Data from industrial insurance companies:		
Policies in force.....	69,851,041	70,648,953
Number of death claims.....	14,460	13,664
Death claims per 1,000 policies in force, annual rate.....	10.8	10.1
Death claims per 1,000 policies, first 4 weeks of year, annual rate.....	10.0	9.6

## FOREIGN REPORTS

### CANADA

*Provinces—Notifiable diseases—Week ended January 7, 1950.—*

During the week ended January 7, 1950, cases of certain notifiable diseases were reported by the Dominion Bureau of Statistics of Canada as follows:

Disease	New-found-land	Prince Edward Island	Nova Scotia	New Brunswick	Quebec	Ontario	Manitoba	Saskatchewan	Alber-ta	Brit-ish Columbia	Total
Chickenpox.....			63	3	99	517	58	101	91	82	1,014
Diphtheria.....	1				5	4			2		12
Dysentery, bacillary.....							2			6	8
Encephalitis, infectious.....							1				1
German measles.....			5		2	107		16	219	49	398
Influenza.....			55			5	9			3	72
Measles.....			20		132	355	50	96	165	219	1,037
Mumps.....			99		14	493	4	3	98	144	855
Poliomyelitis.....				1		1					2
Scarlet fever.....	1		3	2	24	31	11	7	72	10	161
Tuberculosis (all forms).....	7			7	89	23	18	10		45	199
Typhoid and paratyphoid fever.....					2		1				3
Undulant fever.....					1						1
Venereal diseases:											
Gonorrhoea.....	7	2	5	4	135	68	32	16	22	90	381
Syphilis.....	3	1	1	4	37	16	6	4	2	9	93
Other forms.....					2						2
Whooping cough.....	1		28		19	44	3	10	2	4	111

## CHINA

*Cerebrospinal Meningitis and Smallpox.*—Under date of January 21, 1950, a serious epidemic of cerebrospinal meningitis, smallpox, and other diseases were reported in Hsiang-Yang District of north Hupeh. The first fatalities were reported late in December and by early January were spreading south and east from the Lao-Ho-Kou Region. More than 300 deaths occurred in a few days in the region of Hung-Shan.

## CUBA

*Habana—Notifiable diseases—5 weeks ended December 31, 1949.*—Certain notifiable diseases were reported in Habana, Cuba, as follows:

Disease	Cases	Deaths	Disease	Cases	Deaths
Chickenpox.....	2		Measles.....	1	
Diphtheria.....	9		Tuberculosis.....	4	3
Malaria.....	2		Typhoid fever.....	8	

*Provinces—Notifiable diseases—5 weeks ended December 31, 1949.*—Notifiable diseases were reported in the Provinces of Cuba as follows:

Disease	Pinar del Rio	Habana <sup>1</sup>	Matanzas	Santa Clara	Camaguey	Oriente	Total
Cancer.....	8	16	12	29	4	26	95
Chickenpox.....		1	2	2			5
Diphtheria.....	1	9	5	1	2	3	21
Leprosy.....		4		1		1	6
Malaria.....	2	2			6	50	60
Measles.....		1		1	19		21
Tetanus.....		1					1
Tuberculosis.....	6	10	15	8	12	22	73
Typhoid fever.....	4	11	2	4	4	13	38
Whooping cough.....		28			1		29

<sup>1</sup> Includes the city of Habana.

## JAMAICA

*Notifiable diseases—3 weeks ended November 19, 1949, and 5 weeks ended December 31, 1949.*—Cases of certain notifiable diseases were reported in Kingston, Jamaica, and in the island outside of Kingston, as follows:

Disease	3 weeks ended November 19, 1949 <sup>1</sup>		5 weeks ended December 31, 1949	
	Kingston	Other localities	Kingston	Other localities
Chickenpox.....	2	25	3	15
Diphtheria.....	5	3	2	
Dysentery, unspecified.....			1	
Erysipelas.....		2		1
Leprosy.....		1		
Polomyelitis.....		1		1
Tuberculosis (pulmonary).....	37	34	36	39
Typhoid fever.....		37	11	46

<sup>1</sup> Report for week ended November 26, 1949, not received.

## REPORTS OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER RECEIVED DURING THE CURRENT WEEK

NOTE.—The following reports include only items of unusual incidence or of special interest and the occurrence of these diseases, except yellow fever, in localities which had not recently reported cases. All reports of yellow fever are published currently.

A table showing the accumulated figures for these diseases for the year to date is published in the PUBLIC HEALTH REPORTS for the last Friday in each month.

### Cholera

*India.*—During the week ended January 14, 1950, cholera was reported in Calcutta (42 cases with 12 deaths), Negapatam (14 cases with 3 deaths), and Madras (2 cases with 1 death).

### Plague

*Siam (Thailand).*—During the week ended January 7, 1950, one case of plague was reported in Kanburi Province, Siam.

### Smallpox

*Arabia.*—During the week ended January 14, 1950, 19 cases of smallpox were reported in Jedda and 11 cases of smallpox were reported in Mecca.

*Burma.*—During the week ended January 14, 1950, smallpox was reported in Bassein (86 cases), Moulmein (4 cases), and Rangoon (45 cases).

*Indonesia—Java.*—During the week ended January 14, 1950, 19 cases of smallpox were reported in Djakarta, Java. During the week ended January 7, 1950, 16 cases with 1 death were reported in Djakarta.

*Siam (Thailand).*—During the week ended January 14, 1950, 125 cases with 15 deaths were reported in Srisaket Province, Siam.

### Typhus Fever

*Turkey.*—During the week ended January 14, 1950, three cases of typhus fever were reported in Izmir, Turkey.